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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/878,792	06/11/2001	Barbara P. Wallner	10248/7016 ERP	4496

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EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	**PAPER NUMBER**
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/878,792	Applicant(s) WALLNER ET AL.	
	Examiner Jeffrey E. Russel	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-12,16-18,22,30,34,42,52 and 58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12,16-18,22,30,34,42,52 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 June 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. The abstract of the disclosure is objected to because at line 1, "hematopoietic" should be changed to "hematopoiesis" and because at line 2, the comma should be deleted. Also, the Abstract is insufficiently detailed as to the nature of the active agent. Formula I should be recited in the Abstract, and reference should be made to ValboroPro. Correction is required. See MPEP § 608.01(b).

2. The drawings are objected to because in the heading for Figure 9, "Hematopoiesis" is misspelled. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

> An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

In addition, the status of the parent non-provisional application should be updated in the claim for priority in the first sentence of the specification.

4. The disclosure is objected to because of the following informalities: At page 10, lines 4-6, the difference between 1 mg/kg body weight/day and 0.1 mg/kg body weight/day is a factor of about 10, or one order of magnitude. The specification describes this difference as 10 orders of magnitude, or a factor of 10^{10}, which is incorrect. Appropriate correction is required.

5. Claims 1-6, 8-12, 16-18, 22, 30, 34, 42, 52, and 58 are objected to because of the following informalities: Formula I needs to be recited in each of the independent claims which

refers to the formula. Claims are to be complete in themselves, and incorporation by reference is permitted only where there is no other practical way to define the invention. Applicants have not shown that it is impractical to explicitly recite Formula I in the claims. See MPEP 2173.05(s). Appropriate correction is required.

6. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 16-18 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 10-12 of prior U.S. Patent No. 6,300,314. This is a double patenting rejection.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 8-12, 16-18, 22, 30, 34, 42, 52, ad 58 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. 6,300,314. Although the conflicting claims are not identical, they are not patentably

distinct from each other because the claims of the '314 patent anticipate instant claims 1-6, 8-12, 16-18, 22, 30, and 34. With respect to the kits claimed in instant claims 42, 52, and 58, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to provide the inhibitors required by the methods claimed in the '314 patent in a kit containing the inhibitors in unit dosage form and with instructions for use because such kits are routinely used in the pharmaceutical arts for ease of storage and to ensure correct administration of the drug.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

9. Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Bachovchin et al (U.S. Patent No. 5,462,928). Bachovchin et al '928 teaches in vivo administration of compounds of Applicants' Formula I. See, e.g., the claims. Because stromal cells are inherently present in the patients treated in Bachovchin et al '928, then inherently the method of Bachovchin et al '928 will result in stimulated growth factor production by the stromal cells because the same cells are being contacted with the same compounds by the same method steps in Bachovchin et al '928 as are claimed by Applicants.

10. Claims 8, 9, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 94/03055. The WO Patent Application '055 teaches increasing hematopoietic activity and increasing T-cell production by administration of DP-IV inhibitors such as Pro-boroPro. Administration can be intravenously in a dosage of about 1-10 mg/kg/day, or can be orally once or several times daily in a dosage of 1-10 mg/kg/day. Patients being treated include

those undergoing chemotherapy or radiotherapy. See, e.g., pages 9-10, Example 6. With respect to claims 8 and 9, because the WO Patent Application '055 describes administering the inhibitors to patients "undergoing" chemotherapy treatment or to patients "undergoing" radiotherapy, the administration of the inhibitors is deemed to be substantially simultaneous with the chemotherapy or radiotherapy. With respect to claim 34, because stromal cells are inherently present in the patients treated in the WO Patent Application '055, then inherently the method of the WO Patent Application '055 will result in stimulated growth factor production by the stromal cells because the same cells are being contacted with the same compounds by the same method steps in the WO Patent Application '055 as are claimed by Applicants.

11. Claims 1-6, 8-12, 22, 42, 52, and 58 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 94/03055. Application of the WO Patent Application '055 is the same as in the above rejection of claims 8, 9, and 34. With respect to claims 8 and 9, to the extent that the WO Patent Application '055 is not taught to occur prior to or substantially simultaneous with the chemotherapy or radiotherapy, and with respect to claims 3, 22 and 23, where the claimed administration schedule is not taught by the WO Patent Application '055, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal administration schedules for the method of the WO Patent Application '055 because administration schedules are routinely determined and optimized in the pharmaceutical arts. The WO Patent Application '055 does not teach dosages of less than 1 mg/kg/day or the dosages functionally defined in instant claims 4-6, 11, and 12. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal dosages for the method of the WO Patent

Application '055 because dosage is an art-recognized variable which is routinely determined an optimized in the pharmaceutical arts. Note that there is no indication in the WO Patent Application '055 that dosages less than 1 mg/kg/day will not work, that the intravenous dosage range disclosed by the WO Patent Application '055 overlaps Applicants' claimed dosage range because of the word "about", and that the prior art claims directed to this method are not limited to any particular dosage. The difference between the prior art's exemplified dosage range and Applicants' claimed dosage range is minimal, and when the difference between the claimed invention and the prior art is the range or value of a particular variable, then a prima facie rejection is properly established when the difference in the range or value is minor. See Haynes International Inc. v. Jessop Steel Co., 28 USPQ2d 1652, 1655, n. 3 (Fed. Cir. 1993). With respect to instant claims 42, 52, and 58, while the WO Patent Application '055 does not teach its inhibitors in kit form, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to provide the inhibitors of the WO Patent Application '055 in a kit containing the inhibitors in unit dosage form and with instructions for use because such kits are routinely used in the pharmaceutical arts for ease of storage and to ensure correct administration of the drug.

12. Claims 52 and 58 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 95/11689. The WO Patent Application '689 teaches compounds of Applicants' formula I in unit dosage form in amounts which provide a dosage of between 10 and 500 μg/kg/day. See, e.g., page 6, line 11 - page 7, line 4, and page 7, lines 21-34. The WO Patent Application '689 does not teach the unit dosages in kit form, and does not teach the number of dosages present in the kit as claimed by Applicants. It would have been obvious to

one of ordinary skill in the art at the time Applicants' invention was made to package the unit dosages of the WO Patent Application '689 in kit form because such kits are routinely used in the pharmaceutical arts for ease of storage and to ensure correct administration of the drug. It would further have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal number of unit dosage forms to be included in the kit because it would be desirable to ensure that the patient is administered a sufficient amount of the drug but not too much of the drug. An intended use limitation does not impart patentability to composition or article of manufacture claims where the composition or article is otherwise anticipated by or obvious over the prior art.

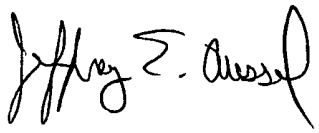
13. Claims 1-3 and 22 are rejected under 35 U.S.C. 103(a) as being obvious over Huber et al (U.S. Patent No. 6,040,145). Huber et al teach stimulating proliferation of T-cells, especially $CD4^+$ and CTL's, both in vivo and in vitro, by administering very low concentrations, on the order of 10^{-8} to 10^{-12} M, of inhibitors of post-prolyl cleaving dipeptidase. A preferred inhibitor is ValBoroPro. The low concentrations of inhibitor used result in low toxicity for the treatment. Treatment results in restoring the T-cell immune response, e.g., against both HIV and other opportunistic pathogens. See, e.g., the Abstract; column 1, lines 40-44; column 1, line 53 - column 2, line 5; column 2, lines 17-19; and column 6, lines 25-36. Huber et al do not teach Applicants' claimed dosages, although the inhibitor concentrations desired by Huber et al are consistent with those disclosed by Applicants (see page 5, lines 15-17, of the specification) and the low toxicity resulting from the low concentrations disclosed by Huber t al is also one of the advantages named by Applicants (see page 10, lines 7-8, of the specification). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to

determine all operable and optimal blood concentrations, and to determine all operable and optimal dosages necessary to achieve these blood concentrations, for the inhibitors of Huber et al because inhibitor blood concentration and inhibitor dosage are art-recognized result-effective variables which are routinely determined and optimized in the pharmaceutical arts. With respect to instant claims 3 and 22, while the claimed administration schedule is not taught by Huber et al, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal administration schedules for the method of Huber et al because administration schedules are routinely determined and optimized in the pharmaceutical arts.

14. Bachovchin et al (U.S. Patent No. 6,258,597) has been carefully considered with respect to instant claim 34, but is not deemed to teach or suggest the claimed invention. While Bachovchin et al teach contacting stromal cells with DPIV inhibitors (see, e.g., column 2, lines 9-11 and 58-60, and column 3, lines 7-11), Bachovchin et al do not teach, inherently or otherwise, contacting the stromal cells with DPIV inhibitors of Applicants' formula I. Further, Bachovchin et al do not teach or suggest that DPIV inhibitors would have any effect on the stromal cells' production of growth factor, and do not provide any motivation to optimize the amounts of DPIV inhibitors in order to stimulate growth factor production by the stromal cells.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

February 7, 2003